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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,673	01/10/2001	James M. Wilson	GNVPN.019B1USA	8771

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EXAMINER	
SHUKLA, RAM R	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/15/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

file

Office Action Summary	Application No. 09/757,673	Applicant(s) WILSON ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10 and 12-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10 and 12-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amendment and response filed 10-30-02 have been received.

2. Amendments to claims 12, 18, 23 and 24 have been entered.

3. Claims 7-10 and 12-24 are pending and under consideration in the instant application.

4. The abstract has been entered.

Claim Objections

5. Objection to claims 18, 23, and 24 has been withdrawn.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 7-10 and 12-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record set forth in the previous office action of 7-30-02.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 7-10 and 12-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record set forth in the previous office action of 7-30-02.

Response to Arguments

Applicants have argued both 112 first and second paragraph rejections together. Accordingly, the applicant's arguments' arguments are responded together.

Applicants have argued that on page 35, lines 1-5 the specification teaches that rAAV purified according to the invention contains no detectable amounts of contaminating adenovirus. However, as noted in the previous office action, the recited phrase encompasses "equal to" or "more" pure recombinant AAV composition compared to the preparation of recombinant AAV obtained after four rounds of cesium chloride centrifugation. However, the specification does not provide written support either for the phrase it self or for equal to or more pure AAV preparation compared to that obtained by four rounds of cesium chloride centrifugation. Regarding applicants' arguments that an artisan could detect the amount of contaminating adenovirus in a rAAV preparation, "no detectable amount" can not provide support for the phrase recited because the "no detectable amount" is a relative term and could defer based on the definition of what is considered detectable. Even if one agreed that the term "no detectable amount" is a definite term, the term "no detectable amount" can only describe the "equal to" part of the recited limitation. If "the equal to" indicates no detectable amount, then what is encompassed by "more" pure than that prepared by four rounds of purification. Therefore, the metes and bounds of the claimed invention are not clear. Applicants arguments that the inventors were first to have found that contamination of rAAV with adenovirus helper virus was responsible for immune response is not relevant to the issue of written description.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214

USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 7-10 and 12-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,866,552 (Wilson JM et al., 2-2-1999) for reasons of record set forth in the previous office action of 11-23-01 and 7-30-02.

11. Claims 7-10 and 12-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 9, 20, 21, 23, 25, 26, and 27 of co-pending Application No. 09/237,064 for reasons of record set forth in the previous office action of 11-23-01 and 7-30-02.

12. Claims 7-10 and 12-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-24 and 26-28 and 30-35 of co-pending Application No. 09/242,977 for reasons of record set forth in the previous office action of 11-23-02 for reasons of record set forth in the previous office action of 11-23-01 and 7-30-02.

Applicants' response that they will file a terminal disclaimer over 552 patent and the co-pending applications 09/237,064 and 09/242,977 is acknowledged.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 7-10, 18 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Podsakoff et al (US 5,858,351, 1-12-1999, filing date 1-18-1996, ref. # AI in the IDS filed 3-16-01) for reasons of record set forth in the previous office action of 11-23-01 and 7-30-02.

Response to Arguments

Applicant's arguments filed 10-30-02 have been fully considered but they are not persuasive. Applicants' argument that Podsakoff does not recognize the contamination with adenoviral helper virus is responsible for an undesired cytotoxic immune response is not persuasive because use of AAV as a gene delivery was realized due to the immune response produced by adenoviral vectors (see lines 50-67 in column 1). Regarding the argument that Podsakoff preparation has contaminating adenovirus remaining in the cesium chloride banded preparation, it is noted that the instantly claimed invention does not recite that the AAV preparation is devoid of helper adenovirus. Regarding the issue of other differences between the preparation of Podsakoff et al and the instant invention, the discussion is not relevant since the claims do not recite these characteristics.

Therefore, the invention of claims 7-10, 18 and 23 is anticipated by Podsakoff et al and the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said

subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 7-10 and 18-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al (US 5,858,351, 1-12-1999, filing date 1-18-1996, ref. # AI in the IDS filed 3-16-01) in view of Kashyap et al. (Journal of Clinical Investigation 96:1612-1620, ref# CU in the IDS filed 3-16-01) for reasons of record set forth in the previous office action of 11-23-01 and 7-30-02.

Response to Arguments

Applicant's arguments filed 10-30-02 have been fully considered but they are not persuasive. Applicants' arguments that Podsakoff's motivation to use rAAV is because muscles cells have insufficient receptors for adenoviruses is not persuasive because they seem to have ignored the discussion in lines 52-56. Additionally, while applicants have argued that Podsakoff preparation has higher contaminating levels of adenovirus, they ignore the fact that the Podsakoff's preparation bands at a density of 1.38 (see lines 30-35 in column 18) whereas that of the instant invention is 1.37-140 (lines 22-23 of page 34 of the specification). This indicates that the preparation of Podsakoff has characteristics similar to that of the instant invention. Additionally, the issue of "no detectable level" as being the indicator of the four rounds of purification indicates that based on the assay used there may be contaminating helper virus or there may not be. This also indicates that by any other assay that may be more sensitive than the 293 cell culture assay, the definition of detectable level will change. Applicants' arguments that the defects of Podsakoff reference are not overcome by Kahsyap reference are not persuasive because the and other limitations are taught by Podsakoff. As noted in the previous office action, teaching of Kashyap considered in the instant case is the DNA encoding ApoE and in view of the benefits of using AAV over adenovirus vector as taught by Podsakoff, an artisan would have used an AAV vector and purified it to make it free of helper virus to minimize immune reaction. Therefore, the rejection of claims 7-10 and 18-24 is maintained.

10. Claims 7-10 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al 1999 in view of Fang et al 1995 (Fang B et al Human Gene Therapy 6:1039-1044, 1995, ref. # CS in the IDS filed 3-126-01) and Kay et al (US 5,980, 886, 11-9-1999) for reasons of record set forth in the previous office action of 11-23-01.

Response to Arguments

Applicant's arguments filed 10-30-02 have been fully considered but they are not persuasive. Applicants' arguments regarding Podsakoff have been addressed in the previous paragraph (#9). It is reiterated that applicants argue that neither of the documents recognize the problem of immune response associated with helper virus contaminations in AAV preparations. Again, applicants are advised to look at Podsakoff , which realizes the problem (see column 1, lines 50-54). It is noted that applicants have emphasized four rounds of purification as the centerpiece of their invention, however, the claims as recited do not recite any specific characteristic of the preparation.

11. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

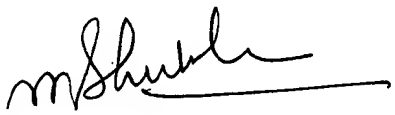
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242.

Ram R. Shukla, Ph.D.



RAM R. SHUKLA, PH.D
PATENT EXAMINER